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#### Declaration under Rule 4.17:

— as to non-prejudicial disclosures or exceptions to lack of novelty (Rule 4.17(v)) for all designations

#### Published:

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments  
— with a declaration as to non-prejudicial disclosures or exceptions to lack of novelty

(88) Date of publication of the international search report:

7 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR DIAGNOSIS OF COLORECTAL TUMORS

(57) Abstract: The invention provides objective methods for detecting and diagnosing colorectal cancers and pre-malignant lesions. For example, the methods disclosed herein can reliably detect very early-stage colorectal cancers. In one embodiment, the diagnostic method involves the scoring of gene expression profiles that discriminate between adenomas and carcinomas. The profile score calculated acts as diagnostic indicator that can objectively indicate whether a sample tissue is non-cancerous, pre-cancerous, or cancerous. The present invention further provides methods of diagnosing colorectal tumors in a subject, methods of screening for therapeutic agents useful in the treatment of colorectal tumors, methods of treating colorectal tumors and method of vaccinating a subject against colorectal tumors.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 02/12760

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 G01N33/50 C12Q1/00 A61K31/7088 A61K39/395  
A61K39/00 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BUCKHAULTS P ET AL: "Secreted and cell surface genes expressed in benign and malignant colorectal tumors"</p> <p>CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 61, 1 October 2001 (2001-10-01), pages 6996-7001, XP002960006</p> <p>ISSN: 0008-5472</p> <p>page 6998, right-hand column, paragraph 4; figures 2, 5B; table 3</p> <p style="text-align: center;">----- -/--</p>	<p>1-14, 16-19</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

27 October 2003

Date of mailing of the international search report

24. 01. 05

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/JP 02/12760

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZHANG L ET AL: "Gene expression profiles in normal and cancer cells" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 276, 23 May 1997 (1997-05-23), pages 1268-1272, XP002083785 ISSN: 0036-8075 table 4	1-14, 16-19
A	----- JI H ET AL: "A TWO-DIMENSIONAL GEL DATABASE OF HUMAN COLON CARCINOMA PROTEINS" ELECTROPHORESIS, WEINHEIM, DE, vol. 18, no. 3/4, 16 September 1996 (1996-09-16), pages 605-613, XP002071493 ISSN: 0173-0835 page 612, right-hand column, paragraph 1; table 1	1
A	----- REYMOND M A ET AL: "STANDARDIZED CHARACTERIZATION OF GENE EXPRESSION IN HUMAN COLORECTAL EPITHELIUM BY TWO-DIMENSIONAL ELECTROPHORESIS" ELECTROPHORESIS, WEINHEIM, DE, vol. 18, no. 15, 1 December 1997 (1997-12-01), pages 2842-2848, XP002071492 ISSN: 0173-0835 page 2846, right-hand column, paragraph 3; table 1	1
A	----- SCHWEINFEST C W ET AL: "Subtraction hybridization cDNA libraries from colon carcinoma and hepatic cancer" GENE ANALYSIS TECHNIQUES, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 7, 1990, pages 64-70, XP002089887 ISSN: 0735-0651 figure 1	1
A	----- EP 0 284 362 A (ICI PLC) 28 September 1988 (1988-09-28) page 8; tables 1-4	1
A	----- WO 98/42736 A (HOCHSTRASSER DENIS FRANCOIS ;REYMOND MARC ANDRE (CH); PROTEOME SCI) 1 October 1998 (1998-10-01) figures 1-3 -----	1

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/JP 02/12760

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 5, 6 and 10-18 are directed to a method of treatment of the human/animal body, or to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-14, 16-19, all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-14, 16-19, all partially

Methods for diagnosing colorectal tumors, screening therapeutic agents, treating or preventing colorectal tumors, vaccinating a subject against colorectal tumors and vaccine compositions relating to the first gene listed in Table 1 (TGFB1).  
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Inventions 2-51: Claims 1-14, 16-19, all partially

Idem as subject 1 but relating to each of the genes listed in Table 1. Invention 2 relates to the second gene listed in Table 1 (IFITM2), invention 3 to the third one (CD81), and so forth.  
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Inventions 52-427: Claims 1-10 and 15, all partially

Idem as subject 1 but relating to each of the genes listed in Table 2. Invention 52 relates to the first gene listed in Table 2 (PFKFB3), invention 53 to the second one (ACHE), and so forth.  
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Inventions 428-459: Claims 4-14, 16-20, 22-24 all partially

Idem as subject 1 but relating to each of the genes listed in Table 3. Invention 428 relates to the first gene listed in Table 3 (IGLL2), invention 429 to the second one (XBP1), and so forth.  
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Inventions 460-477: Claims 4-14, 16-19, 21-24, all partially

Idem as subject 1 but relating to each of the genes listed in Table 4. Invention 460 relates to the first gene listed in Table 4 (COL1A1), invention 461 to the second one (CBX3), and so forth.  
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Inventions (further): Claims 1-24 all partially

Idem as subject 1 but relating to any combination of the genes listed in Tables 1-4. Each combination of genes is considered a further separate invention.  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

Information on Application No

PCT/JP 02/12760

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